

The Journal of Pain

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Volume 16, Number 1, January 2015

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Data Interpretation in Analgesic Clinical Trials With Statistically Nonsignificant Primary Analyses: An ACTION Systematic Review

Jennifer S. Gewandter, Andrew McKeown,
Michael P. McDermott, Jordan D. Dworkin, Shannon M. Smith,
Robert A. Gross, Matthew Hunsinger, Allison H. Lin,
Bob A. Rappaport, Andrew S. C. Rice, Michael C. Rowbotham,
Mark R. Williams, Dennis C. Turk, and Robert H. Dworkin

Peer-reviewed publications of randomized clinical trials (RCTs) are the primary means of disseminating research findings. "Spin" in RCT publications is misrepresentation of statistically nonsignificant research findings to suggest treatment benefit. Spin can influence the way readers interpret clinical trials and use the information to make decisions about treatments and medical policies. This study aimed to determine the frequency with which 4 types of spin were used in publications of analgesic RCTs with nonsignificant primary analyses in 6 major pain journals. Findings highlight a need for authors, reviewers, and editors to be more cognizant of how analgesic RCT results are presented and attempt to minimize spin in future clinical trial publications.

ON THE COVER

These immunohistochemistry images were part of a study published in *The Journal of Pain* that elucidated the analgesic effect of acupuncture in a mouse pain model. The image is provided courtesy of Y Li et al (Li Y, Zhang Haijun, Zhang Hongmei, Kosturakis AK, Jawad AB, Dougherty, PM. Toll-like receptor 4 signaling contributes to paclitaxel-induced peripheral neuropathy. *J Pain* 15:712-725, 2014).

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Original Reports

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Spatial Summation of Pain in Humans Investigated Using Transcutaneous Electrical Stimulation

Emily Reid, Daniel Harvie, Rohan Miegel, Charles Spence, and G. Lorimer Moseley

Spatial summation of pain is well accepted but surprisingly understudied. Area-based summation refers to the increase in pain evoked by increasing the area of stimulation. Distance-based summation refers to the increase in pain evoked by increasing the distance between multiple stimuli. Although transcutaneous electrical stimulation (TENS) has several advantages over other experimental pain paradigms, whether or not this modality evokes spatial summation remains unknown. This study demonstrates that TENS is safe, feasible, and valid for future investigations of spatial summation and will allow critical questions to be answered.

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Subgrouping for Patients With Low Back Pain: A Multidimensional Approach Incorporating Cluster Analysis and the STarT Back Screening Tool

Jason M. Beneciuk, Michael E. Robinson, and Steven Z. George

Early screening for psychological distress has been suggested to improve patient management for individuals experiencing low back pain. This study compared 2 approaches to screening (ie, multidimensional and unidimensional) so that preliminary recommendations on which approach may be appropriate for use in clinical settings could be provided. The STarT Back Screening Tool (SBT) was examined. Results indicate that SBT can replace administering several unidimensional psychological measures as a first-line screening measure for psychological distress. However, clinicians need to be aware of the potential for misclassification with SBT results. Also, patients identified with elevated levels of pain-associated distress and maladaptive coping may be indicated for additional assessment using construct-specific questionnaires.

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A Developmental Analysis of the Factorial Validity of the Parent-Report Version of the Adult Responses to Children's Symptoms in Children Versus Adolescents With Chronic Pain or Pain-Related Chronic Illness

Melanie Noel, Tonya M. Palermo, Bonnie Essner, Chuan Zhou, Rona L. Levy, Shelby L. Langer, Amanda L. Sherman, and Lynn S. Walker

The widely used Adult Responses to Children's Symptoms (ARCS) measures parental responses to child symptom complaints among youth aged 7 to 18 years with recurrent/chronic pain. Given developmental differences between children and adolescents and the impact of developmental stage on parenting, the factorial validity of the parent-report version of the ARCS with a pain-specific stem was examined separately in 743 parents of 281 children (7-11 years) and 462 adolescents (12-18 years). Results suggest that revised structures that differ across developmental groups can be used with youth with a range of clinical pain-related conditions.

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The Associations Between Preexisting Mental Disorders and Subsequent Onset of Chronic Headaches: A Worldwide Epidemiologic Perspective

Ronny Bruffaerts, Koen Demyttenaere, Ronald C. Kessler, Hisateru Tachimori, Brendan Bunting, Chiyi Hu, Silvia Florescu, Josep Maria Haro, Carmen C. W. Lim, Viviane Kovess-Masfety, Daphna Levinson, Maria Elena Medina Mora, Marina Piazza, Patryk Piotrowski, Jose Posada-Villa, Mohammad Salih Khalaf, Margreet ten Have, Miguel Xavier, and Kate M. Scott

Although there is a significant association between preexisting depression and later onset of chronic headache, the extent to which other preexisting mental disorders are associated with subsequent onset of headache in the general population is not known. Also unknown is the extent to which these associations vary by gender or by life course. This study shows that there is a temporal association between a broad range of preexisting mental disorders and the subsequent onset of severe or frequent headaches in general population samples across the world. It also highlights the importance of assessing a broad range of mental disorders.

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Transcranial Magnetic Stimulation Reveals Cortical Hyperexcitability in Episodic Cluster Headache

Giuseppe Cosentino, Filippo Brighina, Sara Brancato, Francesca Valentino, Serena Indovino, and Brigida Fierro

Cluster headache (CH) is an extremely painful headache disease, clinically impressing with strictly unilateral pain accompanied by ipsilateral cranial autonomic symptoms. The headache attacks typically occur in cluster periods lasting several weeks or months, separated by remission periods of months or years. Evidence shows involvement of the cerebral cortex in the pathophysiology of CH. The authors investigated cortical excitability in episodic CH patients by using transcranial magnetic stimulation. The study concludes that an abnormal state of cortical excitability could be involved in the pathophysiology of the disease.

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Plasma Membrane Mechanisms in a Preclinical Rat Model of Chronic Pain

Luiz F. Ferrari and Jon D. Levine

The authors have shown that the prolongation of prostaglandin E₂ hyperalgesia in a preclinical model of chronic pain—hyperalgesic priming—is mediated by release of cyclic adenosine from isolectin B4-positive nociceptors and its metabolism by ectonucleotidases to produce adenosine. This study further contributes to the understanding of mechanisms involved in the organization of messengers at the plasma membrane that participate in the transition from acute to chronic pain.

67 Peripheral Group I Metabotropic Glutamate Receptor Activation Leads to Muscle Mechanical Hyperalgesia Through TRPV1 Phosphorylation in the Rat

Man-Kyo Chung, Jongseok Lee, John Joseph, Jami Saloman, and Jin Y. Ro

Elevated glutamate levels within injured muscle play important roles in muscle pain and hyperalgesia. In this study, the authors hypothesized that protein kinase C (PKC)-dependent TRPV1 phosphorylation contributes to the muscle mechanical hyperalgesia following activation of Group I metabotropic glutamate receptors (mGlu1/5). This article demonstrates that activation of mGlu1/5 leads to phosphorylation of a specific TRPV1 residue via PKC and AKAP150 in trigeminal sensory neurons and that functional interactions between glutamate receptors and TRPV1 mediate mechanical hyperalgesia in the muscle tissue.

77 Effectiveness of Jyoti Meditation for Patients With Chronic Neck Pain and Psychological Distress—A Randomized Controlled Clinical Trial

Michael Jeitler, Stefan Brunnhuber, Larissa Meier, Rainer Lütke, Arndt Büssing, Christian Kessler, and Andreas Michalsen

Chronic neck pain is a common medical complaint partly mediated by psychosocial distress and having a high socioeconomic impact. There is preliminary evidence that stress reduction by meditation might be beneficial in chronic pain syndromes. An 8-week meditation program (jyoti meditation) was examined in patients with chronic neck pain by means of a randomized clinical trial. Meditation training significantly reduced pain when compared to the group assigned to a home-based exercise program. In conclusion, meditation reduced pain at rest but not disability and might be a useful treatment option for pain management of chronic neck pain.

87 Motor Cortical Activity During Motor Tasks Is Normal in Patients With Complex Regional Pain Syndrome

Gijsbrecht A. J. van Velzen, Johan Marinus, J. Gert van Dijk, Erik W. van Zwet, Inger B. Schipper, and Jacobus J. van Hilten

Motor dysfunction in complex regional pain syndrome (CRPS) is often considered a functional movement disorder. Earlier studies in patients with functional movement disorders found evidence of cortical inhibition during explicit but not during implicit motor tasks, suggesting active inhibition from other brain areas. This study explored whether active inhibition occurs in CRPS patients. Such patients were compared with 2 control groups: healthy controls matched for age and sex, and patients whose hand was immobilized to treat a scaphoid fracture. Results show that motor dysfunction in CRPS patients differs from that encountered in patients with functional paresis or under circumstances of limb immobilization. This information is important for patients and pain clinicians and could help prevent implementation of therapeutic strategies based on incorrect assumptions.

Reviewer Acknowledgments

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